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REPORT NO. 86-15

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Report No. 86-15, supported by the Naval Medical Research and Development Command, Department of the Navy, under research Work Units MR04101.03-0161 and MF58528.02-0001. The views presented in this paper are those of the authors. No endorsement by the Department of the Navy has been given or should be inferred. The authors wish to thank the Commanding General, the staff, and personnel of the Marine Corps, Camp Pendleton, California, for their cooperation and help with this study. In addition, the authors note with gratitude the participation of the Commanding Officers and personnel of the 1st Battalion, 5th Marine Division, and the 1st Battalion, 7th Marine Division.

The authors thank Marion Austin, Matthew Sinclair, Lorene Irwin, HM3 Robert Parrish, USN, HM3 David McCormick, USN, Michael Genhart, Steven Gomez, Simone Ballinger, and Julie Bellune for their contributions in the areas of technical planning, data collection, and data analysis, and Marcia Lucas for her invaluable editorial assistance. The authors acknowledge with appreciation the contributions of Timothy H. Monk, Ph.D., and Laverne C. Johnson, Ph.D., to the development of the protocol for this study.

SUMMARY

The conduct of military operations may involve rapid deployment across multiple time zones, altered work-rest schedules, and performance under conditions of sleep loss. We evaluated the sleep-promoting effects of the amino acid l-tryptophan in the field in this study of the acute effects of rapid deployments on performance.

Subjects were 51 Marines (age 21 ± 2.2 years) airlifted from California to Okinawa. Physiological data were obtained from 12 subjects using Medilog recorders. Subjective measures included analog mood scales, the Stanford Sleepiness Scale, and the Profile of Mood States. Performance measures included 4-choice reaction time (RT), and addition task (AT), the Williams Word Memory Test (STM), and the Digit Symbol Substitution Test (DSST). Baseline data were collected 2 weeks prior to deployment on 3 consecutive days (B1, B2, B3), on the 2 days immediately prior to the flight, the day of flight, and 2 days after arrival (O1, O2). Target shooting performance was assessed one week prior to departure and on O1, both sessions at 0800 LT. L-tryptophan 2 g or placebo was administered en route and on the first 3 nights in Okinawa. To maximize sleep during flight, environmental interventions included timing of meals and other inflight activities, elimination of caffeine, and control of cabin lighting. Acute "jet-lag" effects were assessed by comparing data for B3, O1, and O2 at 0900, 1500, and 2100 LT by ANOVA for repeated measures. Post-hoc t-tests were used to identify sources of significant effects. For target shooting, factors were treatment group (placebo or l-tryptophan) and day. Between-groups t-tests were used to compare total sleep for l-tryptophan and placebo subjects.

On the first night in Okinawa, total nighttime sleep time was significantly increased in the l-tryptophan group (274.5 ± 19.9 min versus 222.3 ± 44.8, t=2.16, p<.0315, one-tailed). Our RT test, a very sensitive measure of fatigue, showed treatment differences with placebo subjects having significantly slower RT at 2100 on O1 (t=2.28, p<.0308, two-tailed). Mean sleep time aboard the aircraft was 291 ± 79 min for placebo subjects and 324 ± 146 min for l-tryptophan subjects. This 33-minute difference was not statistically significant. After arrival, evening performance showed the deleterious effects of "jet lag". DSST and AT recovered by O2. STM showed a progressive deterioration from the time of arrival through the evening of O2. There was a consistent pattern in the various subjective measures of significantly poorer mood and increased sleepiness on O1 particularly in the evening. By O2, mood had recovered in the daytime but was still significantly worse at 2100 compared to B3. Target shooting mean scores were significantly lower on O1 (28.2 ± 10.5 versus 21.2 ± 9.8, t=4.37, p<.0001, two-tailed).

"Jet lag" may be considered to be the result of multiple factors. Our interventions greatly reduced the impact of sleep-loss effects associated with this deployment. The inflight environmental controls increased sleep during transit; data collected earlier in a pilot study showed mean sleep time en route to be only 2 ± 1.2 h, when environmental controls were not employed and no pills were given. L-tryptophan administration increased total sleep time on the first night after arrival, and this increase in sleep was associated with faster reaction time in the evening the following day. In addition, l-tryptophan use appeared to spare short-term memory from jet-lag effects and hastened the

recovery of reaction-time performance. As far as we are aware, this study is the first demonstration that improving sleep by psychopharmacological means is associated with enhanced performance the next day. Previous research on westward flight has indicated that readjustment occurs relatively quickly, particularly in young, military subjects. Our data show "jet-lag" effects on mood and performance on the first day after arrival with most dramatic decrements in the evening test battery. Many measures show changes which might be interpreted as the beginning of readjustment as early as the second day.

INTRODUCTION

This Center Report is the first of several reports and scientific articles describing the effects of jet lag on performance and presenting interventions to minimize performance degradation. The goal of this Report is to present as simply and as clearly as possible our results regarding the effects of westward rapid deployment on performance and mood and the efficacy of l-tryptophan as a sleeping aid for operational use in jet-lag conditions. Later articles will focus on more theoretical issues, describe more complex statistical approaches, and will raise more basic research questions.

Jet lag was identified as an important mission factor in a letter written by the Commandant of the Marine Corps, Headquarters, United States Marine Corps, Washington, DC. In his letter, he requested the continuation of research on interventions for managing jet-lag effects. His letter specifically described the possible usefulness of the amino acid l-tryptophan in promoting sleep after time-zone crossings (CMC ltr MED:DRH:plm 6500 9Jun83). More recently, the Commander, Naval Sea Systems Command, Washington, DC, requested development of biomedical technology, specifically mentioning pharmacologic techniques, to provide support in special forces missions (Commander, NSSC ltr 6440 Ser 06Z/094 28Aug84). The current research program is responsive to both tasking documents.

Jet Lag: An Overview

The term "jet lag" is a colloquialism which refers to a syndrome associated with air travel. The syndrome takes different forms and may include both psychological effects and physiological changes (Klein et al., 1972; Aschoff, 1976; Wright et al., 1983; Winget et al., 1984). The possible adverse effects of time-zone crossings were first described in 1931 by the pilot Wiley Post, who set a world record for a solo flight around the world (Post and Gatty, 1931). Jet lag involves sleep problems, gastrointestinal distress, and most notably, fatigue at inappropriate times of the day at destination (Klein et al., 1976; Desir et al., 1981). Jet lag has received considerable attention, both in terms of scientific study and popular articles, and has been the subject of several books. The research studies attempt to document changes associated with transmeridian flight and to come to some understanding of the causes of those changes as well as their functional significance. Considerable attention has been focused on developing ways to combat jet-lag effects (Ehret et al., 1978; Graeber et al., 1981; Ehret and Scanlon, 1983). Among these techniques are special diets, shifting in advance to the new local time, remaining on home time after arrival, and the ingestion of certain amino acids or vitamins. From the military point of view, the question becomes: Is jet lag an operational problem? How significant is the crossing of time zones to military personnel's ability to function effectively at destination? In the present study, we documented changes in various kinds of performance and mood and also tested intervention techniques designed to alleviate performance loss associated with jet lag.

Conceptually, jet-lag effects may be seen as the result of at least three factors. The first of these is sleep loss. It has been well-documented over the years that prolonged sleep deprivation over time

results in changes in mood and performance. (For an overview, see Johnson and Naitoh, 1974; Nicholson et al., 1984.) In situations requiring multiple time-zone crossings, sleep loss may occur in at least three ways. During the period of preflight preparation, the individual may sleep less than usual because of demands on his/her time. Also, there may be a preparatory anxiety, eagerness, or interest about the impending travel, as well as farewell parties and alcohol consumption, which may result in sleep loss. On most commercial flights going westward, the traveler's day is lengthened, and the number of hours of sleep in a 24-h period is reduced. On most commercial overnight eastward flights, total sleep time is reduced because of the difficulty in obtaining restorative sleep aboard the aircraft. In addition to these factors, it may be easy to fall asleep at the local bedtime following westward travel, but difficult to stay asleep throughout the night. After eastward travel, on the other hand, it might be difficult to go to sleep at the local bedtime and awaken at the local arousal time.

The second major factor contributing to the jet-lag effect is clock time differences. Body rhythms are synchronized to a 24-h clock, and each body function shows a peak and a trough over the 24-h day. When an individual is time-locked to the environment, various physiological rhythms are in synchrony, even though the peaks and troughs in different functions may occur at different times in the 24-h day. One factor in jet lag is the eventual discrepancy between the body's clock and the clock on the wall (Aschoff, 1976; Wegmann et al., 1983), the "external desynchronosis" described by Fuller et al., (1981). After arrival, some rhythms remain temporarily locked to the local time at origin, and, therefore, performance and mood and other functions do not bear their appropriate relationship to the new local time. One of the questions to be asked about jet-lag effects is this: Are the changes seen simply the result of the discrepancy between environmental time and biological time? Or, is performance at destination a function of biological time as well as some other important kind of degrading effect?

After arrival at destination, a third factor contributing to the jet-lag effect becomes important. This factor has been called "internal desynchronosis" (Fuller et al., 1981). As soon as the new environmental and the social cues become apparent, biological rhythms will begin to migrate toward the new local time. In some cases, the flight itself may cause a change in the biological clock; for example, we suspect that, as you travel westward and stay in daylight longer, the biological clock will begin to shift. During readjustment, these rhythms become disjointed and out of synchrony, as various functions conform to the new time, more or less quickly (Desir et al., 1981; Wegmann et al., 1983). This period of desynchronosis is often associated with poor mood, sleeplessness, and performance changes (Hauty and Adams, 1966; Klein et al., 1972; Aschoff, 1976; and Graeber et al., 1981). For certain functions, performance and mood might get worse before they get better as biological rhythms begin to adjust to the zeitgebers at destination. Jet lag, then, may have both an acute phase and a more long-term phase for different functions.

There have been several previous studies of jet-lag effects on military personnel (Adam et al., 1972; Klein et al., 1976; Graeber et al., 1981; Wright et al., 1983). Overall, these studies agree that military personnel experience less disruption and more rapid readjustment of circadian rhythmicity

following multiple time-zone crossings than do civilian populations. While translocated soldiers report the subjective fatigue, sleepiness, and irritability which typically follow transmeridian travel, the readjustment rates of the mean oral temperature cycle and simple addition and auditory performance rhythms are faster than those usually observed in civilian populations (Adam et al., 1972; Colquhoun, 1979; Graeber et al., 1981). It is hypothesized that the rapid post-flight readjustment rates found in studies of military personnel are facilitated by the extensive experience in transmeridian deployment (Graeber et al., 1981), increased motivation (Klein et al., 1976; Graeber et al., 1981), and cohesive social networks characteristic of military populations (Adam et al., 1972; Graeber et al., 1981).

Because of the rigid performance demands placed upon military personnel immediately following transmeridian flight, studies have been conducted to test the effectiveness of techniques to minimize jet-lag effects. In two military studies by Graeber et al. (1981), rest-activity schedules, social cues, light-dark cycles, meals, and caffeine consumption were controlled to induce a more rapid post-flight adjustment of circadian rhythms in translocated soldiers. The effectiveness of these countermeasures under difficult field conditions was manifest in decreased fatigue and desire to sleep, improved information processing and concentration, faster temperature rhythm adaptation, greater encoding-decoding task completion, and preservation of post-flight performance levels.

L-tryptophan as a Sleeping Aid

Since sleep loss is hypothesized to be an important part of the jet-lag effect, it may seem obvious that administration of a sleeping aid to maximize sleep during transit or at destination is an appropriate intervention. We have been particularly interested in the sleep-inducing properties of an amino acid called l-tryptophan. L-tryptophan is regularly ingested in the diet as a constituent of protein foods and is well-represented in milk. Many people believe that a glass of milk at bedtime will help one fall asleep more quickly. We have done two studies in the laboratory evaluating the sleep-enhancing effects of l-tryptophan.

In one study, we asked day workers to take naps for us during the normal work-day. Subjects took either l-tryptophan 4 g or placebo an hour before their naps, and we used EEG procedures to measure sleep latency (the time from lights out until Stage 2 onset). L-tryptophan reduced daytime sleep latency by approximately one-third (Spinweber et al., 1983). Daytime naps are a good model for jet lag, since going to sleep at destination may be similar to taking a nap during your normal working hours because of the time-zone shift.

In a nighttime study, the sleep-promoting effects of l-tryptophan 3 g were assessed in a group of chronic, sleep-onset insomniacs (Spinweber, 1986). In this study, l-tryptophan reduced sleep latency significantly on the fourth through sixth nights of administration. It appeared that, in chronic insomniacs, three nights of pretreatment with l-tryptophan were needed before hypnotic effects became evident. L-tryptophan administration did not produce performance loss at any time after administra-

tion. We also evaluated arousal threshold, that is, how loud a tone must be to awaken the sleeper, and found that l-tryptophan did not make it more difficult to wake up after sleep onset. We also evaluated short- and long-term memory for word lists and found that l-tryptophan did not impair recall or recognition performance. The effects of l-tryptophan on responsivity during sleep, post-administration performance, and memory were evaluated in our study because the more commonly used benzodiazepine hypnotics adversely affect these measures.

Military Operation

The Marine Corps, in its unit deployment concept, currently airlifts whole battalions from Camp Pendleton, California (located approximately 30 miles north of San Diego), to Okinawa, Japan, for 6-month training missions. In a given week, two 747 flights transit from San Diego to Okinawa, and, during the same week, two flights return from Okinawa carrying a second battalion home. We conducted this study on the first westbound flight from San Diego to Okinawa during one of these week-long military operations. The westbound flight is approximately 15 h air time plus a 2-h stop in Anchorage, Alaska. (See Figure 1.) Local time in Okinawa is 17 h ahead of California Pacific Standard Time (PST). In this study, we obtained data before, during, and after the flight to assess acute jet-lag effects and to evaluate the hypnotic efficacy of l-tryptophan in the field.

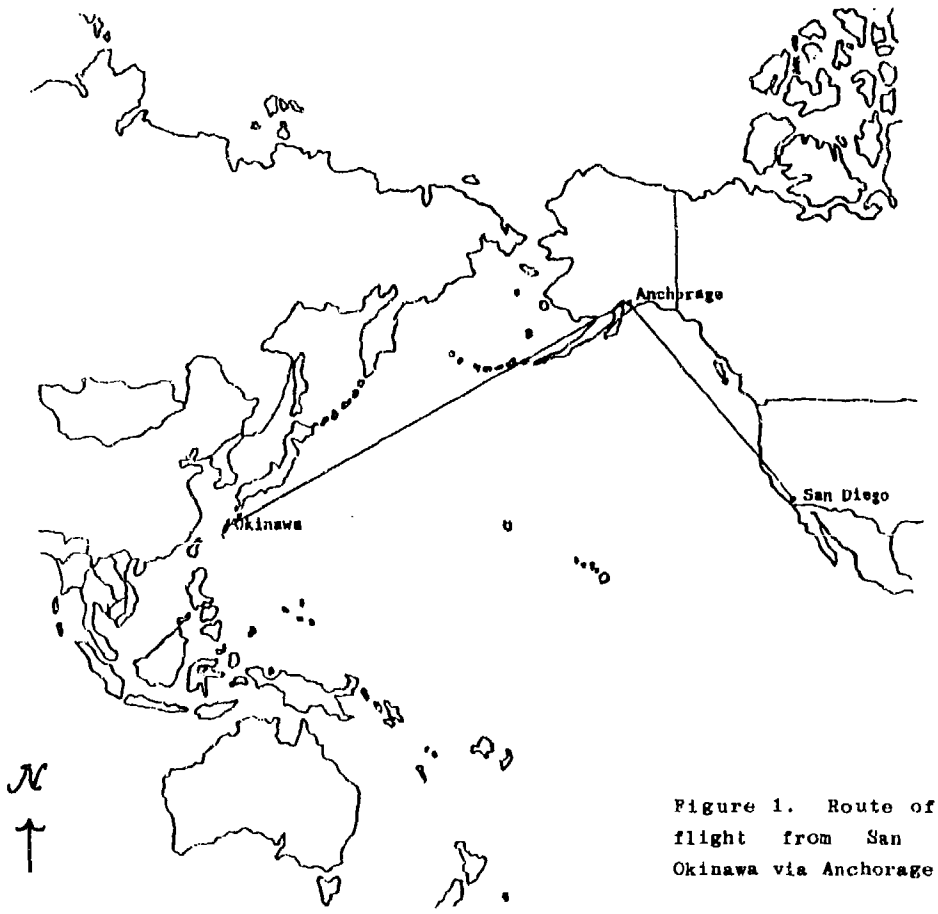


Figure 1. Route of westward flight from San Diego to Okinawa via Anchorage, Alaska.

METHOD

Our research study involved two phases. The first phase was a pilot study in which we became familiar with this major troop movement, collected pilot data from one battalion, and had the opportunity to field-test our methods. Two months later, an operational trial was conducted. In this report, the main emphasis is on the results of the operational trial, but reference is made occasionally to pilot data.

Subjects

Potential subjects were Marines at Camp Pendleton, California, who were scheduled for deployment to Okinawa, Japan. Pilot data were collected from 27 Marine volunteers from the 1st Battalion, 5th Marine Division (1/5) (mean age 21.7 $\pm$ 3.2 years). The operational trial was conducted with 51 Marine volunteers from the 1st Battalion, 7th Marine Division (1/7) (mean age 21.0 $\pm$ 2.2 years).

Procedure

Operational Trial: The testing schedule for the operational trial is summarized in Table 1. Baseline data were collected 2 weeks prior to deployment on 3 consecutive days (B1, B2, and B3) at 0900 and 1500. On B3, in addition to the 0900 and 1500 batteries, an evening test battery was conducted at 2100. Also on B3, subjects were required to remain awake after the evening test battery until after another battery was conducted at 0300. The 4 test batteries scheduled on B3 provided comparison data for the day of the flight (F). Two days of preflight data (P1, P2) were collected at 0900 and 1500. During flight, only subjective measures and oral temperature were obtained. Arrival at Okinawa was at 1730 local time. An evening test battery was conducted at 2200. Testing on the first 3 full days (O1 and O2) in Okinawa was at 0900, 1500, and 2100. The study ended at 0800 on the third morning.

Batteries 1-12 were conducted in the battalion mess hall at Camp Pendleton. Batteries 13-15 were conducted aboard the aircraft. Batteries 16-23 were conducted in a classroom at Camp Hansen in Okinawa. There was some deviation in the established testing schedule, as follows: battery 14 actually occurred at 1600 PST; battery 15 at 2330 PST; battery 16 at 2200 Okinawa LT; and battery 17 at 1000. Delays in batteries 14-15 were due to the inflight activities; battery 16 was delayed because of military requirements after arrival; and battery 17 was delayed because of the extra time it took subjects to return from the firing range.

Target shooting performance was assessed one week prior to departure and on O1. Both target shooting sessions occurred at 0800 local time. Stationary targets were used. The target consisted of 3 silhouettes. Subjects were permitted one practice round on the left and right silhouette and permitted to adjust their weapon sights. Then, each subject was allowed 8 rounds on the center silhouette. Accuracy was scored using a bull's-eye scoring system with a total possible accuracy

score of 40 points. Each subject used his own M16 rifle on both days. A total of 45 subjects provided target scoring data in both locations.

Table 1.

TEST SCHEDULE

Battery	Study Day	San Diego Time	Okinawa Time
1	B1[1]	Mon 0900	
2	B1	Mon 1500	
3	B2	Tue 0900	
4	B2	Tue 1500	
5	B3	Wed 0900	
6	B3	Wed 1500	
7	B3	Wed 2100	
8	B3	Thu 0300	
	(two weeks intervening time)		
9	P1[2]	Mon 0900	
10	P1	Mon 1500	
11	P2	Tue 0900	
12[6]	P2	Tue 1500	
13[6]	F[3]	Wed 0900[5]	
14[6]	F	Wed 1500[5]	
15[6,7]	F	Wed 2100[5]	
16[7]	F		Thu 2100[5]
17	O1[4]		Fri 0900[5]
18[7]	O1		Fri 1500
19	O1		Fri 2100
20	O2		Sat 0900
21[7]	O2		Sat 1500
22[6]	O2		Sat 2100
23	O3		Sun 0600

[1] "B" indicates baseline days, 2 weeks prior to departure week.
[2] "P" indicates days immediately prior to the flight day.
[3] "F" indicates day of the flight.
[4] "O" indicates days immediately following the day of flight.
[5] Battery was delayed due to other requirements (see text).
[6] Subjective measures and oral temperature only were obtained.
[7] L-tryptophan 2 grams administered at the conclusion of the test battery.

L-tryptophan 2 g or placebo was administered en route after reboarding at Anchorage and on the first 3 nights in Okinawa at approximately 2200, following the evening test batteries. To maximize sleep during flight, environmental interventions included timing of meals and other inflight activities, no caffeine, and control of cabin lighting. These controls were as follows:

All subjects sat in the forward cabin of the 747.

Meal service was conducted after take-off from San Diego and again immediately after take-off from Anchorage.

One movie was shown, immediately after meal service during the Anchorage-Okinawa flight segment only.

Snacks and beverages were offered only to awake individuals.

No caffeine was ingested aboard the aircraft (i.e., no coffee, tea, soda containing caffeine, chocolate milk, chocolate candy, etc.). Beverages without caffeine could be ingested, including decaffeinated coffee, herbal tea, Pepsi Free, juice, milk, or water.

Window shades were down and cabin lights off during the Anchorage-Okinawa flight segment from conclusion of meal service until 1 h prior to arrival. Window shades could be up and lights on during the San Diego-Anchorage flight segment.

Before departure, troops were encouraged to maximize sleep throughout the trip.

Performance Measures

Performance measures included a test of reaction time, the Wilkinson 4-Choice Reaction Time Test (RT); a decoding task, the Digit Symbol Substitution Test (DSST); a test of short-term memory, the Williams Word Memory Test (STM); and a test involving math calculations, the Wilkinson Addition Test (AT). All tests chosen were known to be sensitive to sleep deprivation and to drug effects.

RT: Fifteen 4-Choice Reaction Time Recorders were obtained from KE Developments, Cambridge, England. The apparatus consists of a cassette tape recorder, having 4 red lights and 4 white buttons, which correspond in position to one of the red lights. When turned on, the apparatus would illuminate 1 red light. Each subject was instructed to press the white button corresponding in position to the illuminated red light. Whenever the subject pressed a button, whether correct or incorrect, the illuminated light would shut off. Automatically, a light would be illuminated in a randomly-determined fashion, and the subject was again to press the correct button to turn off the light. Task duration was 15 min. Subjects were instructed to work as quickly and accurately as possible (Wilkinson and Houghton, 1975). Because of equipment limitations, 30 subjects provided RT data in the study.

Responses were recorded on cassette tape and later analyzed by a PDP-11/34 computer for average reaction time for each performance battery.

STM: In this test, different 15-word lists were presented at each test battery. The experimenter first said the word, then spelled the word, then said the word again. Subjects wrote each word down. When all 15 words had been presented, the subject was allowed 2 min to write down as many of the words he could recall in any order. The score for each test equaled the number of words correctly recalled (Williams and Williams, 1966).

AT: The Wilkinson Addition Test required the addition of columns of 5 2-digit numbers. Test scores were the number of sums attempted and the number correctly calculated. Subjects performed this test

for 15 min, and were urged to work as quickly, but as accurately, as possible (Wilkinson et al., 1966; Wilkinson, 1969).

DSST: The Digit Symbol Substitution Test used was the standard version from Wechsler Adult Intelligence Test (Wechsler, 1955). In this test, subjects were requested to write the appropriate symbol in a box beneath the corresponding number. The test was performed for 90 sec, and the score was the number of items properly decoded.

Subjective Mood Measures

Analogue Mood Scales (AMS): This scale is a paper-and-pencil version of the computerized Visual Analogue Scales developed by Monk and co-workers (Monk et al., 1985). It consists of nine uni-directional scales ranging from "very little" to "very much" along a 100 cm line. The separate scales ask, "how alert do you feel", "how sad", "how tense", "how happy", "how weary", "how calm", and "how sleepy"; "how much of an effort is it to do anything?"; and "overall, how do you feel"? The subject was instructed to draw a line on the 100 cm line to reflect his present feelings. The datum for each scale was number of cm's from the left hand margin.

Profile of Mood States (POMS): The POMS is a mood test consisting of 65 adjectives to which the subject makes one of four responses ranging from "not at all" to "extremely". Subscale scores for tension, depression, anger/hostility, vigor, fatigue, and confusion/bewilderment (McNair et al., 1971) were dependent measures.

Stanford Sleepiness Scale (SSS): The SSS is a 7-item scale which requests that the subject report how he is feeling at the present time. Each time the SSS was administered, the subject chose one of the following descriptions (Hoddes et al., 1973):

1. Feeling active and vital; alert; wide awake.

2. Functioning at a high level, but not at peak; able to concentrate.

3. Relaxed; awake, responsive, but not at full alertness.

4. A little foggy; let down; not at peak.

5. Foggy; slowed down; beginning to lose interest in remaining awake.

6. Sleepy; woozy; prefer to be lying down; fighting sleep.

7. Almost in reverie; sleep onset soon; losing struggle to remain awake.

Physiological Monitoring

In both phases of data collection, 12 subjects wore devices for ambulatory monitoring of physiological processes. We used the Medilog 9-channel recorder available from Oxford Medilog, Inc. The following physiological parameters were recorded: Left/right EOG, C4 referred to A1, C3 referred to A2, O1 referred to A2, skin temperature from an ancillary placement, EKG from two chest electrodes, and chest impedance. In addition, a time code and an event marker channel were used. Medilog subjects wore the devices continually during waking and during sleep. Cassette tapes and batteries were changed once every 24 hours. For baseline data collection, Medilogs were applied and recordings begun on B1 and removed after the 0300 test session on B3. During the week of flight, Medilog electrodes were attached and recordings begun two days before the flight. Medilogs were removed after the 23rd test battery at the end of the study. Medilog tapes were later played back on the system scanner and scored for the presence of waking or sleep (Stages 2, 3, 4 or REM) by human scorers. In this report, only the results of analysis of the EEG for total sleep time will be described. Later reports will focus on analysis of temperature rhythms, EKG rhythms, respiration, and other physiological factors.

Data Analysis

Local Time Approach: One approach to assessment of acute jet-lag effects is to measure and compare data for the same time of day at Camp Pendleton and at Okinawa. Test batteries were scheduled at 0900, 1500, and 2100 on B3 to provide baseline data for comparison with Okinawa data for the same time of day. These comparisons hold local time (LT) of day constant and provide information about what kinds of jet-lag effects are to be expected if activities are scheduled according to the local time at destination. Statistically, jet-lag effects were evaluated by comparing data for B3, O1, and O2 at 0900, 1500 and 2100 LT by ANOVA for repeated measures with factors treatment group (G) (placebo/l-tryptophan), day (D) and time (T). Conservative Geisser-Greenhouse (1958) corrections were used to evaluate the significance of F tests. If there were significant effects in the ANOVA, further analyses were performed. In order to determine if there was an overall change on O1 or O2 from baseline, overall day means were derived for each subject for each day by averaging over the 0900, 1500, and 2100 test battery for the day. Post hoc t-tests were used to determine whether day means were statistically different. Further analyses included comparisons of morning, afternoon, and evening test batteries on B3 with O1 and with O2. For target shooting, ANOVA factors were G and D. Between-groups t-tests were used to compare total sleep for l-tryptophan and placebo subjects, as there were no baseline differences in daily sleep between the two Medilog groups.

When the treatment group factor was determined in the omnibus ANOVA to be nonsignificant as a main effect or interaction, data were collapsed over groups as appropriate to give a more clear picture of the jet-lag effects.

Biological Time Approach: This approach, contrastingly, holds biological time (BT) of day constant. We used this approach in the analyses of these data to determine the source of performance and mood

changes that were found through the LT approach. The question asked in this approach was whether performance and mood measures were still locked to PST (biological time) and for how long after arrival. Our study design was structured to permit us to compare Okinawa data with Camp Pendleton data that was within an hour of the identical BT as follows: comparisons for the O1 and O2 0900 batteries were made with the 1600 battery data from B3, the 1500 O1 and O2 batteries with the 2100 B3 data, and the 2100 O1 and O2 batteries with the 0300 battery from B3. Day means were also derived appropriately for B3, using the 1600, the 2100, and the 0300 batteries. The statistical analyses proceeded as described above.

Additional Statistical Notes: Other analyses for specific variables or time periods are described in the RESULTS section. All tests are two-tailed unless otherwise stated. Because of missing data, dfs are indicated and differing dfs reflect differing numbers of data points available. Two of the 51 subjects were dropped from analyses of performance and mood data because of noncompliance with test instructions during several test batteries.

Mean data for all performance and mood measures for all test batteries were first plotted and inspected for baseline differences. In addition, between-groups t-tests were used to locate any baseline differences between groups. Only two subjective measures, "happy" on the AMS and the vigor subscale on the POMS, showed baseline between-groups differences. These differences were also present in the LT ANOVA which showed significant effects of group, as well as significant day and day-by-time interactions. The effect of group in both cases was not a treatment effect, since throughout the protocol, the l-tryptophan group reported more "happiness" and having more vigor even during baseline on B3, before any pills had been administered. These 2 subjective measures were not included in any analyses of treatment group comparisons, although they are presented in discussion of overall jet-lag effects. Because of the lack of baseline differences on other measures, comparison between treatment groups was straightforward, as described above.

RESULTS

Sleep Management

Environmental Controls: The control of the aircraft environment dramatically increased sleep en route in the operational trial compared to those in the pilot study. Pilot study Medilog subjects only obtained 120.0 ± 72 min sleep aboard the aircraft. The range was 16 min of sleep in one subject to a maximum of 3 h 52 min in another. Total sleep time during the operational trial was 291.3 ± 79.2 min for placebo subjects and 324.3 ± 145.9 min for l-tryptophan subjects. This 33-min difference in total sleep time between the 2 groups was not statistically significant. The range of sleep times was 2 to 7 h.

L-tryptophan: L-tryptophan subjects obtained significantly more sleep on the first night in Okinawa compared to placebo subjects (X = 274.5 ± 19.9 min vereus X = 222.3 ± 44.8 min t = 2.16, p<.0314), but not on subsequent nights.

Acute Effects of Flight

Comparison of Treatment Groups Upon Arrival: T-test comparisons between l-tryptophan subjects and placebo subjects showed few significant differences at the time of battery 16. The l-tryptophan subjects had higher mean self-reported alertness (44.7 ± 28.1 versus 31.3 ± 14.4, t(47) = 2.09, p<.0425), and a more positive mean rating of overall mood (44.4 ± 23.2 versus 31.5 ± 17.2, t(47) = 2.20, p<.0327) on the AMS. There were no performance differences between the two treatment groups upon arrival.

Performance Upon Arrival: To determine the acute effects of flight upon performance, battery 16 performance data were compared with battery 7 data and, separately, with battery 8 data using t-tests for correlated means. Results of these comparisons are presented in Tables 2 and 3. The comparisons with battery 7 provide a LT analysis and, with battery 8, a BT analysis. Inspection of mean data on Table 2 indicates that DSST showed essentially no decrement upon arrival. STM means suggest some slight impairment upon arrival but, for both the DSST and STM tasks, comparisons of battery 16 data with battery 7 and battery 8 data showed no statistically significant differences. For AT, performance upon arrival resembled battery 8 performance and, in fact, differed significantly from battery 7. For RT, performance upon arrival was significantly slower than both battery 7 and battery 8 mean reaction times.

Table 2.

EFFECTS OF FLIGHT ON PERFORMANCE

Measure	Battery 7 2100 LT Pendleton X̄ (±SD)	Battery 8 0300 LT Pendleton X̄ (±SD)	Battery 16 2200 LT Okinawa X̄ (±SD)	t^1	$p<^1$	t^2	$p<^2$
DSST (score)	65.2 (10.6)	64.6 (12.1)	63.8 (15.3)	0.80	0.4265	0.52	0.6084
AT (attempted)	68.5 (16.6)	56.7 (18.1)	52.7 (25.2)	6.46	0.0001	1.86	0.0686
AT (# correct)	59.3 (16.0)	47.8 (17.7)	43.6 (25.6)	8.00	0.0001	1.94	0.0587
STM (# correct)	9.5 (2.0)	9.8 (2.0)	8.9 (2.8)	1.34	0.1852	1.73	0.0905
RT (msec)	412.8 (89.8)	518.5 (166.1)	688.9 (443.6)	3.39	0.0021	2.46	0.0210

[1] Comparison of battery 7 and battery 16.
[2] Comparison of battery 8 and battery 16.

Mood Upon Arrival: Evaluation of the acute effects of flight on subjective mood proceeded similarly. For subjective measures, battery 16 data looked quite different from battery 7 data. As seen in Table 3, all t-test comparisons between battery 7 and battery 16 were highly significant. Overall, there were fewer significant differences between subjective mood upon arrival and subjective mood reported at 0300 on B3 at Camp Pendleton. Notably, reported alertness, effort required, weariness, sleepiness, and fatigue were similar upon arrival at 2200 to those at 0300 LT at Camp Pendleton. Measures which may reflect more the psychosocial difficulties encountered upon arrival including customs, a drug information lecture, and a rather long bus ride to Camp Hansen, were significantly worse than battery 8 measures. These reports included being more sad, more tense, less calm, having a poorer overall mood, and more depression and anger.

Table 3.

EFFECTS OF FLIGHT ON SUBJECTIVE MOOD

Measure	Battery 7 2100 LT Pendleton $\bar{X}$ (±SD)	Battery 8 0300 LT Pendleton $\bar{X}$ (±SD)	Battery 16 2200 LT Okinawa $\bar{X}$ (±SD)	t^1	$p<^1$	t^2	$p<^2$
SSS	2.5 (1.2)	4.4 (1.3)	4.9 (1.2)	10.49	0.0001	2.69	0.0098
Alert[3]	63.7 (26.4)	40.0 (27.5)	38.2 (23.2)	6.27	0.0001	0.54	0.5940
Sad[3]	16.8 (20.8)	27.1 (28.8)	33.9 (30.0)	5.04	0.0001	2.07	0.0442
Tense[3]	20.3 (20.3)	23.4 (24.2)	33.6 (29.2)	3.42	0.0013	2.49	0.0162
Effort[3]	29.0 (24.9)	56.2 (29.5)	56.9 (23.4)	7.19	0.0001	0.18	0.8605
Happy[3]	58.6 (26.2)	40.5 (28.0)	34.6 (26.0)	6.39	0.0001	1.52	0.1339
Weary[3]	30.4 (25.8)	61.9 (31.5)	58.9 (27.5)	6.34	0.0001	0.73	0.4672
Calm[3]	64.0 (29.2)	62.1 (30.8)	48.1 (30.7)	3.88	0.0003	2.50	0.0158
Sleepy[3]	35.2 (28.2)	72.3 (28.1)	73.6 (22.2)	8.84	0.0001	0.35	0.7269
Overall Mood[3]	70.7 (21.7)	50.7 (24.2)	38.0 (21.3)	8.96	0.0001	3.93	0.0003
Tension[4]	5.1 (4.2)	7.1 (4.8)	8.3 (4.4)	4.76	0.0001	1.75	0.0861
Depression[4]	4.0 (7.1)	5.9 (9.0)	8.9 (9.1)	4.56	0.0001	2.45	0.0181
Anger[4]	4.5 (7.5)	6.7 (9.5)	12.0 (11.7)	5.00	0.0001	3.18	0.0026
Vigor[4]	12.3 (7.2)	6.2 (5.4)	5.0 (5.7)	7.73	0.0001	2.32	0.0246
Fatigue[4]	3.0 (4.1)	10.9 (7.3)	10.3 (6.2)	7.87	0.0001	0.64	0.5263
Confusion[4]	4.4 (3.2)	7.2 (5.0)	7.4 (4.6)	4.69	0.0001	0.35	0.7264

[1] Comparison of battery 7 and battery 16.
[2] Comparison of battery 8 and battery 16.
[3] From Analogue Mood Scales.
[4] From POMS.

Performance Measures--LT Analyses

RT: Mean RT data for the l-tryptophan and placebo groups are presented in Figure 2. Complete RT data for all test batteries were available for 13 of 15 l-tryptophan subjects and 11 of 15 placebo subjects. Because of missing data, the ANOVA results can only be considered to be suggestive of the kinds of effects influencing the data. The ANOVA for repeated measures on subjects having complete data showed a significant day-by-time interaction ($F(4,88) = 8.17$, $p<.0001$), a significant main effect of time ($F(2,44) = 10.24$, $p<.0002$), and a trend toward group differences ($F(1,22) = 2.96$, $p<.0993$). Post hoc t-tests were used to compare treatment groups. These tests showed that l-tryptophan subjects had significantly faster reaction times than placebo subjects at 2100 on D1.

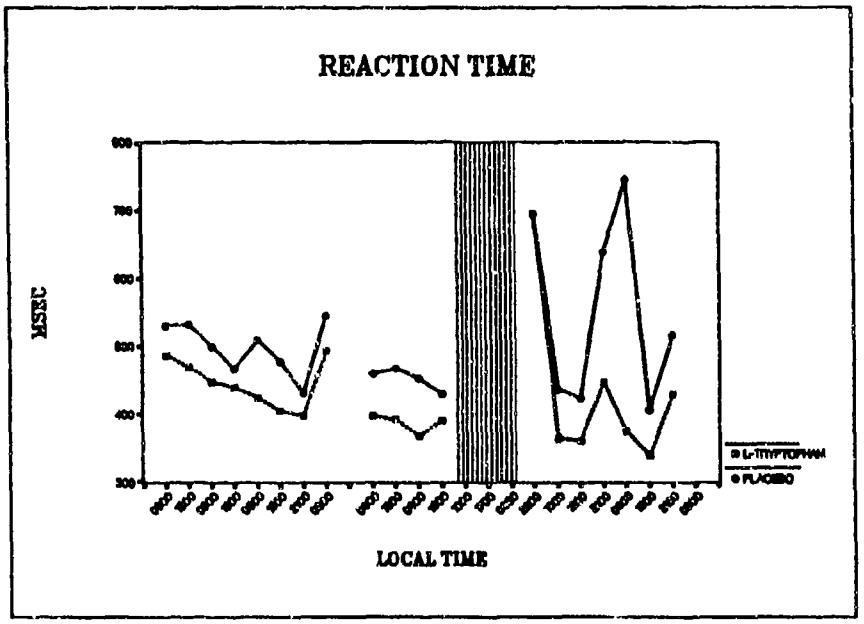
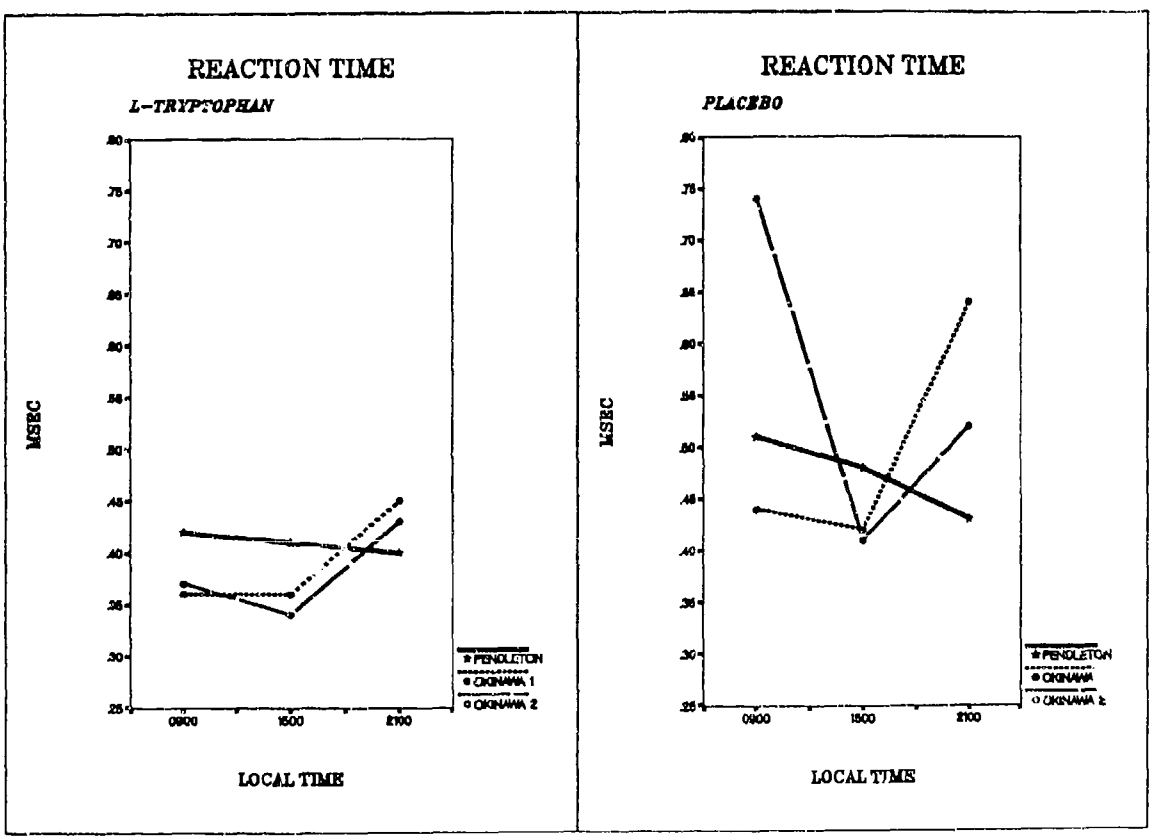


Figure 2. Mean reaction time (RT) on the 4-choice Reaction Time Test for the l-tryptophan and placebo groups separately for all test sessions.

Figures 3a and b show RT means for 0900, 1500, and 2100 on B3, O1, and O2 for each treatment group, separately. In addition to the between-groups difference described above, we note from these figures that the l-tryptophan group's mean RTs showed little change over time, while the placebo group showed a slowing at 0900 on O1 as well as at 2100 on O2.



Figures 3a and b. Mean reaction time (RT) on 4-choice Reaction Time Test at 0900, 1500, and 2100 on study days B3, O1, and O2 for l-tryptophan and placebo groups, separately.

STM: Mean STM data for all performance batteries are presented in Figure 4. The 3-day ANOVA showed a significant main effect of day ($F(2,86) = 4.03$, $p<.0213$), a significant day-by-group interaction ($F(2,86) = 4.56$, $p<.0131$), a significant main effect of time ($F(2,86) = 9.59$, $p<.0002$), and a significant day-by-time interaction ($F(4,172) = 4.31$, $p<.0024$). The significant day-by-treatment group interaction was due to the fact that, compared to baseline, performance in the l-tryptophan group did not decline on O1 and O2, while performance in the placebo group showed a within-group impairment on both days.

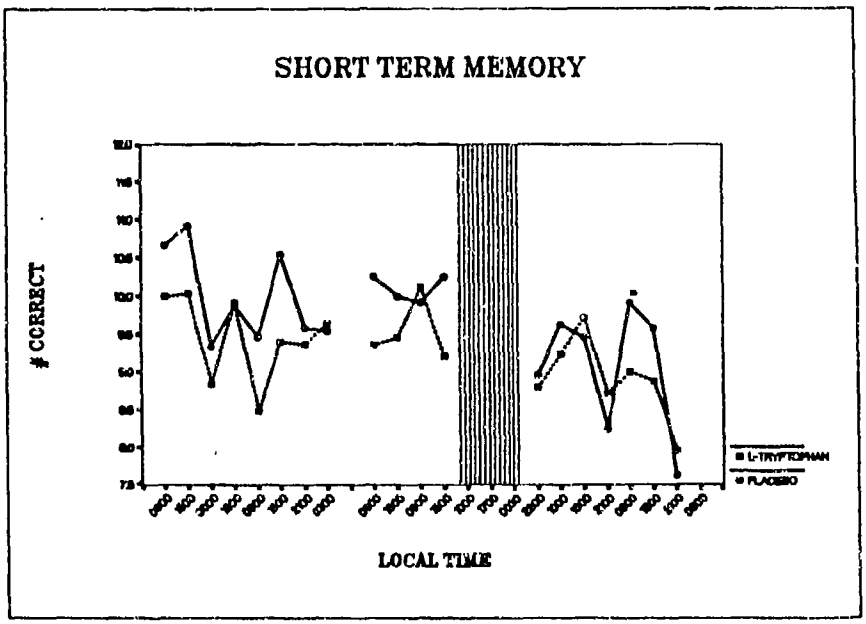
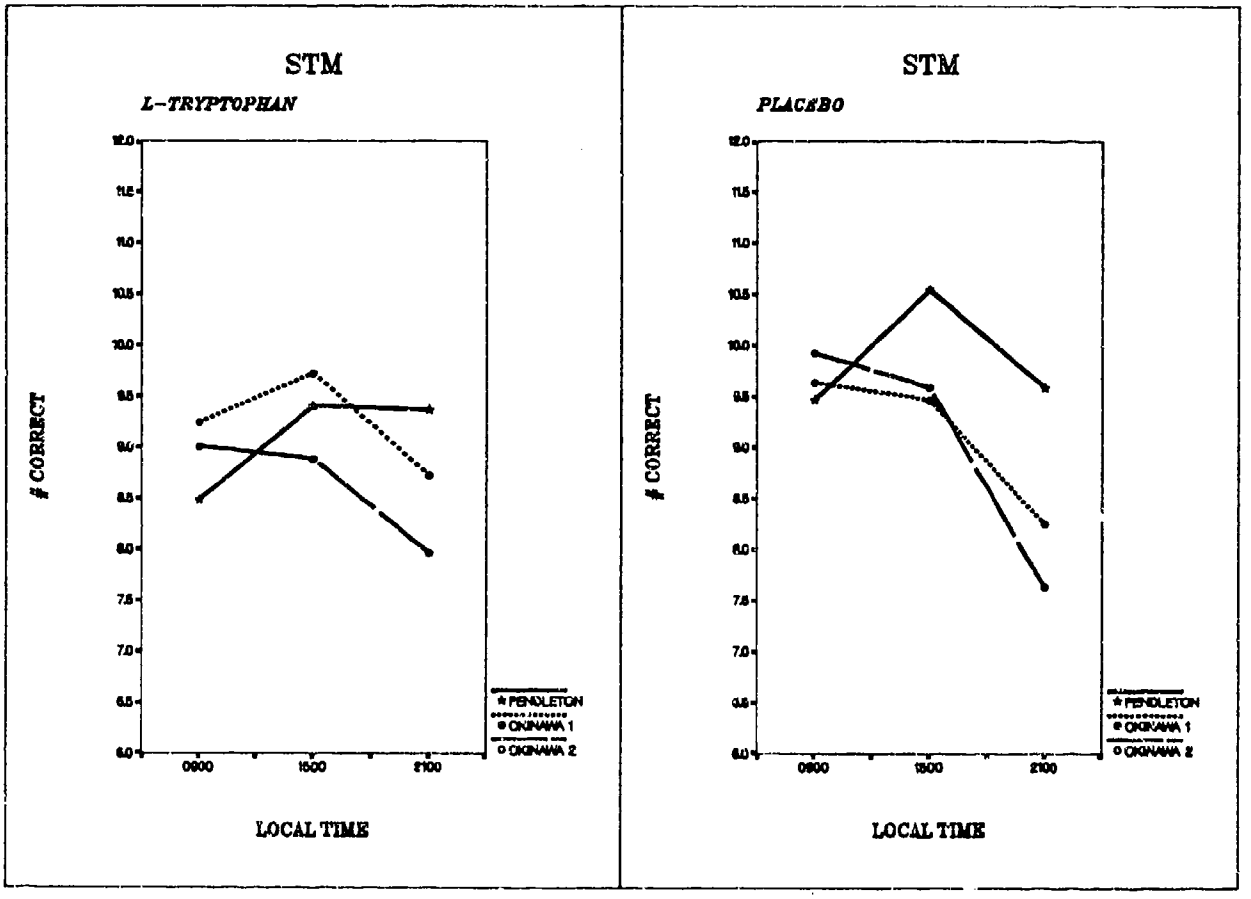


Figure 4. Mean number correct on the Williams Word Memory Test (STM) for the l-tryptophan and placebo groups separately for all test sessions.

The overall day means on STM for l-tryptophan subjects were 9.1, 9.2, and 8.7 for B3, O1, and O2, respectively; for the placebo group, the comparable day means were 9.9, 9.1, and 9.0. As can be seen in Figures 5a and b, in the l-tryptophan group, the evening decrement in STM performance was not present on O1 but did show up on O2. The placebo group curves for O1 and O2 were highly similar to each other and the evening decrement was present on both days.

Combining all subjects' data for B3 and O2, we found that the overall day mean for O2 (8.85 ± 1.71) was significantly lower than baseline (9.46 ± 1.78, $t(47) = 2.85$, $p<.0065$). When comparable LTs were compared, the t-test analyses showed that STM performance was impaired on O2 at 2100 compared to B3, $t(47) = 4.15$, $p<.0001$), but was not significantly different from B3 at 0900 and 1500. We also noted an overall downward trend in STM performance after arrival in Okinawa, as can be seen in Figure 4.



Figures 5a and b. Mean number correct on the Williams Word Memory Test (STM) at 0900, 1500, and 2100 on study days B3, O1, and O2 for l-tryptophan and placebo groups, separately.

AT: Mean data for AT performance are presented in Figure 6. The 3-day ANOVA showed a significant main effect of day ($F(2,86) = 11.55$, $p<.0001$), a significant main effect of time ($F(2,86) = 6.24$, $p<.0029$), and a significant day-by-time interaction ($F(4,172) = 26.89$, $p<.0001$). The overall means for B3, O1, and O2 were 54.9 $\pm$ 15.7, 58.1 $\pm$ 18.8, and 61.0 $\pm$ 18.4, respectively. The B3-O1 difference for the overall day means was significant ($t(47) = 2.32$, $p<.0245$) as was the B3-O2 comparison ($t(47) = 4.89$, $p<.0001$). Means for 0900, 1500, and 2100 are presented in Figure 7. On O1, AT performance was significantly better than baseline at 0900 ($t(48) = 3.73$, $p<.0005$) and at 1500 ($t(48) = 7.29$, $p<.0001$), reflecting the apparent learning curve in the data. AT performance, was significantly worse at 2100 ($t(47) = 4.26$, $p<.0001$), compared to B3. On O2, AT performance was also higher at 0900 ($t(48) = 9.56$, $p<.0001$) and at 1500 ($t(48) = 4.61$, $p<.0001$). The B3-O2 comparison for the 2100 battery was not significant.

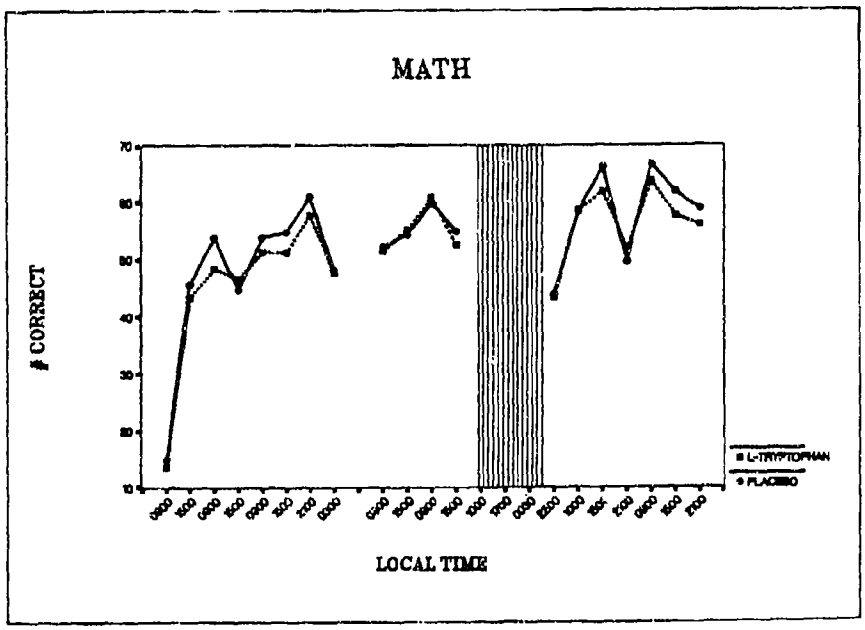


Figure 6. Mean number correct on the Wilkinson Addition Test (AT) for the l-tryptophan and placebo groups separately for all test sessions.

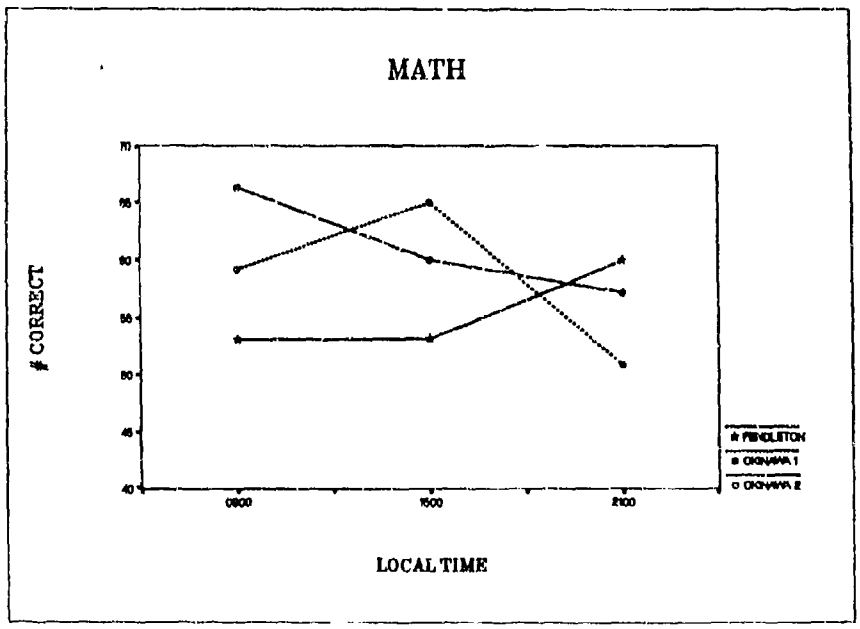


Figure 7. Mean number correct on the Wilkinson Addition Test (AT) at 0900, 1500, and 2100 on study days B3, O1, and O2.

DSST: DSST mean data for all performance batteries are presented in Figure 8. In Figure 8, we see a clear learning curve in DSST performance which continues even after the 2-week break which occurs between battery 8 and battery 9. The effect of the flight is clearly a change in the slope of the data plotted in Figure 8. Results of ANOVA showed a significant main effect of day ($F(2,86) = 35.69$, $p<.0001$), of time ($F(2,86) = 12.70$, $p<.0001$), and a significant time-by-day interaction ($F(4,172) = 7.21$, $p<.0001$). The day means for B3, O1, and O2 were 64.3 $\pm$ 10.0, 67.6 $\pm$ 11.9, and 72.4 $\pm$ 10.8, respectively. The B3-O1 difference was significant ($t(46) = 3.08$, $p<.0035$) as was the B3-O2 difference ($t(45) = 9.92$, $p<.0001$). Compared to B3, on O1, performance was significantly higher at 0900 ($t(48) = 7.49$, $p<.0001$) and at 1500 ($t(48) = 4.82$, $p<.0001$) and not significantly different at 2100. On O2, performance was significantly better at 0900 ($t(48) = 10.01$, $p<.0001$), at 1500 ($t(48) = 6.68$, $p<.0001$), and at 2100 ($t(45) = 4.15$, $p<.0001$). (See Figure 9.) It is important to note that, from inspection of Figure 8, data from B3 may not be the best baseline for this measure since performance continues to improve on study days P1 and P2. Since no 2100 battery was obtained on P1 and P2, we were unable to evaluate the battery 16 and battery 19 performance on this measure in a satisfactory fashion.

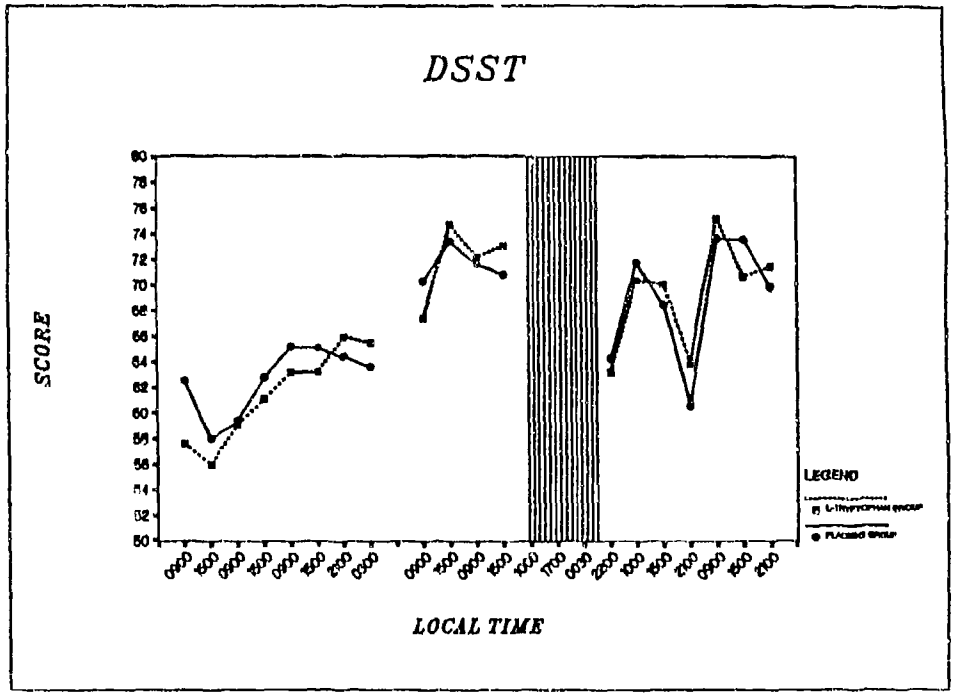


Figure 8. Mean score on the Digit Symbol Substitution Test (DSST) for the l-tryptophan and placebo groups separately for all test sessions.

Target Shooting: At Camp Pendleton, the mean accuracy score for the entire group was 29.2 $\pm$ 10.5, and at Okinawa, the mean score was 21.2 $\pm$ 9.8. The F value for the group effect was not significant: for the repeated measure, $F(1,42) = 19.49$, $p<.0001$.

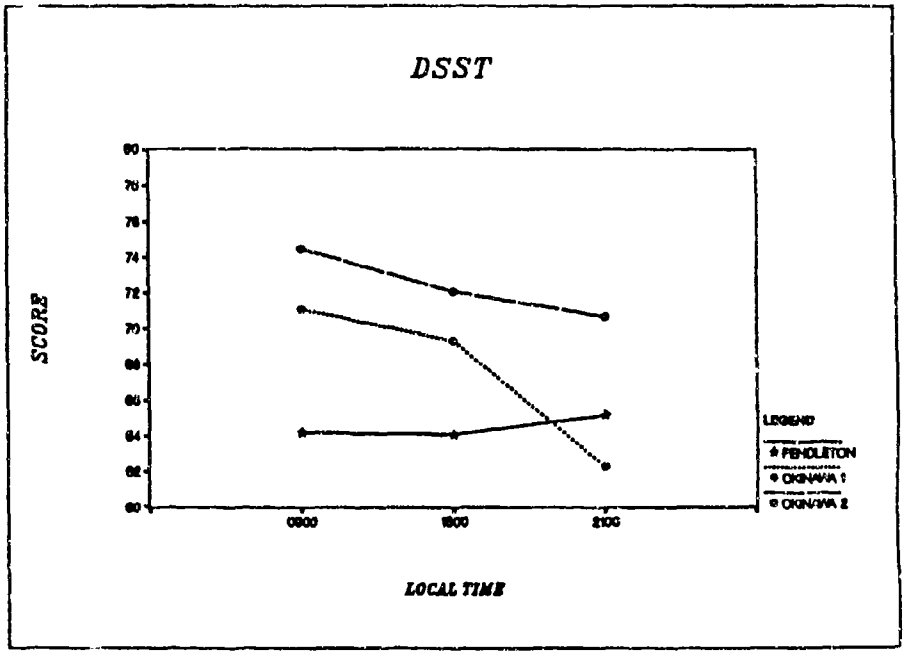


Figure 9. Mean score on the Digit Symbol Substitution Test (DSST) at 0900, 1500, and 2100 on study days B3, 01, and 02.

Percentage Decrement: In order to quantify the degree of performance loss occurring in the evenings according to LT, the numerical change in mean performance at the time of arrival and on each of the two subsequent evenings was compared to the mean performance obtained during battery 7. Results are presented in Table 4a for the DSST, AT, and STM. The calculations were based on all subjects, collapsed over treatment groups. The target shooting percentage decrement was 33%.

Table 4a.

PERFORMANCE LOSS (PERCENT DECREMENT)

Task	Upon Arrival[1]	After 1 Day[2]	After 2 Days[3]
DSST	2.1%	4.4%	-8.4%[4]
AT (attempted)	23.1%	13.9%	3.2%
AT (# correct)	26.0%	14.5%	3.2%
STM	6.3%	10.5%	17.9%

[1] Battery 16 compared to battery 7.
[2] Battery 19 compared to battery 7.
[3] Battery 22 compared to battery 7.
[4] The negative value indicates that the mean performance score in Okinawa was higher than that of the baseline mean at 2100 on B3.

For RT, in which treatment-group differences were present, the comparable percentages for the placebo subjects were 61.3%, 48.4%, and 19.9%. For l-tryptophan subjects, the percentage decrements were 72.6%, 12.2%, and 7.7%.

for comparison, percentage decrement values were also computed using battery 8 data as baseline providing a BT approach by comparing 0300 LT on B3 with the evening test batteries in Okinawa. These results are presented in Table 4b.

Table 4b.

PERFORMANCE LOSS (PERCENT DECREMENT)

Task	Upon Arrival[1]	After 1 Day[2]	After 2 Days[3]
DSST	1.2%	3.6%	-9.4%[4]
AT (attempted)	7.1%	-4.1%[4]	-17.0%[4]
AT (# correct)	8.8%	-6.1%[4]	-20.1%[4]
STM	7.3%	11.5%	18.8%

[1] Battery 16 compared to battery 8.
[2] Battery 19 compared to battery 8.
[3] Battery 22 compared to battery 8.
[4] The negative values indicate that the mean performance score in Okinawa was higher than that of the baseline mean at 0300 on B3.

Subjective Mood Measures--LT Analyses

Because of the large number of subjective variables, only two variables, SSS and "effort" from the AMS, will be presented in detail in a narrative form. Results of analyses of other measures are summarized in Tables 5, 6, and 7.

Table 5.

SUBJECTIVE MOOD DATA

Overall Day Means

Local Time Analyses

	Pendleton (B3) X (±SD)	Okinawa (O1) X (±SD)	Okinawa (O2) X (±SD)	t^1	$p<^1$	t^2	$p<^2$
SSS	2.5 (1.1)	3.6 (1.0)	2.6 (1.0)	5.70	0.0001	1.07	0.2909
Alert[3]	60.7 (21.2)	52.4 (20.1)	63.5 (20.8)	3.54	0.0009	1.05	0.2994
Sad[3]	20.5 (19.0)	33.9 (27.7)	30.2 (27.9)	4.68	0.0001	3.27	0.0020
Tense[3]	23.7 (17.9)	33.4 (21.9)	27.9 (24.2)	3.97	0.0002	1.60	0.1154
Effort[3]	29.6 (20.2)	42.4 (22.8)	31.9 (22.0)	4.25	0.0001	0.56	0.5804
Happy[3]	53.2 (24..)	38.8 (24.3)	53.6 (25.4)	5.17	0.0001	0.01	0.9900
Weary[3]	34.5 (23.7)	41.6 (23.1)	30.6 (23.1)	2.25	0.0292	1.01	0.3178
Sleepy[3]	38.8 (22.4)	52.2 (19.6)	34.8 (21.8)	4.22	0.0001	1.27	0.2093
Overall[3]	66.2 (18.7)	51.9 (19.7)	65.6 (18.5)	5.49	0.0001	0.38	0.7086
Tension[4]	5.7 (3.8)	7.8 (4.5)	6.4 (4.8)	3.54	0.0010	1.24	0.2204
Depression[4]	4.0 (6.2)	9.0 (9.9)	6.4 (8.9)	3.50	0.0011	1.82	0.0756
Anger[4]	5.0 (6.1)	9.9 (10.1)	6.9 (9.7)	3.18	0.0027	1.33	0.1903
Vigor[4]	11.7 (6.8)	7.3 (6.2)	10.1 (6.7)	5.74	0.0001	2.06	0.0446
Fatigue[4]	4.2 (4.5)	7.5 (8.1)	4.2 (5.6)	3.43	0.0013	0.19	0.8490
Confusion[4]	4.7 (2.9)	6.4 (4.0)	5.3 (3.9)	3.44	0.0013	1.11	0.2711

[1] Comparison of B3 and O1.
[2] Comparison of B3 and O2.
[3] From Analogue Mood Scales.
[4] From POMS.

Table 6.

SUBJECTIVE MOOD DATA

Local Time Analyses

	Pendleton (B3)			Okinawa (O1)			Okinawa (O2)		
	0900	1500	2100	0900	1500	2100	0900	1500	2100
	X (±SD)	X (±SD)	X (±SD)	X (±SD)	X (±SD)	X (±SD)	X (±SD)	X (±SD)	X (±SD)
SSS	3.0 (1.3)	2.8 (1.3)	2.5 (1.2)	3.1 (1.1)	2.9 (1.2)	4.8[1] (1.3)	2.4[2] (1.1)	2.2[2] (1.1)	3.2 (1.4)
Alert[3]	58.7 (24.5)	59.9 (25.5)	63.7 (26.4)	60.9 (25.7)	60.8 (24.8)	34.9[1] (22.3)	67.9[2] (24.0)	67.2 (26.7)	53.7[2] (27.0)
Sad[3]	20.9 (21.8)	23.8 (25.9)	16.8 (20.8)	30.1[1] (27.8)	31.8[1] (28.8)	40.6[1] (34.2)	30.4[2] (30.0)	30.0 (29.1)	30.5[2] (29.2)
Tense[3]	24.7 (20.7)	26.2 (24.5)	20.3 (20.4)	29.9 (24.7)	32.9[1] (27.8)	38.3[1] (29.2)	28.6 (26.6)	26.2 (24.3)	30.4[2] (28.5)
Effort[3]	32.7 (25.3)	27.1 (24.0)	29.1 (25.0)	37.4 (27.8)	36.8[1] (26.8)	54.3[1] (27.8)	27.6 (24.7)	27.0 (23.7)	41.8[2] (27.7)
Happy[3]	51.2 (27.1)	49.9 (30.1)	58.6 (26.2)	43.2[1] (30.0)	40.2[1] (28.6)	31.9[1] (24.0)	53.9 (28.4)	53.1[2] (28.7)	53.1 (28.7)
Weary[3]	36.5 (27.1)	36.5 (28.4)	30.4 (25.9)	39.9 (28.0)	39.0 (28.5)	47.9[1] (30.4)	28.4[2] (25.1)	27.7[2] (22.7)	36.4 (28.5)
Sleepy[3]	41.8 (27.0)	39.4 (25.1)	35.2 (28.2)	42.8[1] (26.5)	44.1 (27.6)	71.7[1] (25.3)	31.5[2] (26.0)	29.0[2] (23.8)	44.6[2] (28.1)
Overall[3]	65.4 (21.5)	62.5 (22.9)	70.7 (21.7)	57.7[1] (24.4)	56.5 (23.6)	41.0[1] (24.3)	67.0 (22.7)	67.1 (19.4)	61.9[2] (21.8)
Tension[4]	6.0 (3.8)	6.0 (4.5)	5.1 (4.2)	7.3[1] (5.0)	7.4[1] (4.9)	8.4[1] (5.8)	6.4 (5.3)	6.3 (5.3)	6.7[2] (4.7)
Depression[4]	4.5 (8.0)	4.4 (7.4)	4.0 (7.1)	7.6[1] (9.6)	8.7[1] (10.5)	10.8[1] (12.3)	6.6 (9.7)	6.4 (10.3)	6.6[2] (5.4)
Anger[4]	5.1 (5.0)	5.9 (8.7)	4.5 (7.5)	7.9[1] (10.1)	9.6[1] (10.8)	12.5[1] (12.7)	6.9 (9.9)	7.7 (11.6)	7.0[2] (10.1)
Vigor[4]	11.6 (7.6)	11.3 (7.3)	12.3 (7.2)	8.5[1] (7.2)	8.0[1] (7.3)	5.1[1] (5.3)	10.9 (7.6)	10.9 (7.4)	8.0[2] (6.6)
Fatigue[4]	4.5 (5.1)	5.0 (5.8)	3.0 (4.1)	6.3 (6.1)	6.2 (6.9)	10.0[1] (7.4)	3.5 (6.1)	3.4 (5.7)	5.7[2] (6.7)
Confusion[4]	5.1 (3.3)	4.9 (3.8)	4.4 (3.2)	5.7 (4.4)	6.2 (4.1)	7.5[1] (4.9)	5.2 (4.0)	5.5 (4.6)	5.4 (3.8)

[1] Significant difference between B3 and O1, p<.05 or better, at the same local time.
[2] Significant difference between B3 and O2, p<.05 or better, at the same local time.
[3] From Analogue Mood Scales.
[4] From POMS.

Table 7.

SUBJECTIVE MOOD DATA

Overall Day Means

Biological Time Analyses

	Pendleton (B3)	Okinawa (O1)	Okinawa (O2)	t^1	$p<^1$	t^2	$p<^2$
	X (±SD)	X (±SD)	X (±SD)				
SSS	3.2 (1.0)	3.6 (1.0)	2.6 (1.0)	2.67	0.0103	4.15	0.0001
Alert[3]	54.5 (22.6)	52.4 (20.1)	63.5 (20.8)	0.92	0.3613	3.17	0.0027
Sad[3]	22.5 (21.8)	33.9 (27.7)	30.2 (27.9)	4.27	0.0001	2.64	0.0112
Tense[3]	23.3 (18.3)	33.4 (21.9)	27.9 (24.2)	3.99	0.0002	1.54	0.1299
Effort[3]	37.4 (19.9)	42.4 (22.8)	31.9 (22.0)	1.71	0.0932	1.86	0.0697
Happy[3]	49.7 (23.9)	38.8 (24.3)	53.6 (25.4)	4.06	0.0002	1.11	0.2722
Weary[3]	43.0 (23.5)	41.6 (23.1)	30.6 (23.1)	0.15	0.8823	3.45	0.0012
Sleepy[3]	48.9 (22.8)	52.2 (19.6)	34.8 (21.8)	1.20	0.2345	4.29	0.0001
Overall[3]	61.3 (19.4)	51.9 (18.7)	65.6 (18.5)	3.50	0.0010	1.34	0.1879
Tension[4]	6.1 (4.0)	7.8 (4.5)	6.4 (4.8)	2.67	0.0105	0.48	0.6320
Depression[4]	4.4 (7.0)	9.0 (9.9)	6.4 (8.9)	3.01	0.0043	1.37	0.1765
Anger[4]	5.5 (7.4)	9.9 (10.1)	6.9 (9.7)	2.64	0.0114	0.84	0.4039
Vigor[4]	9.9 (6.0)	7.3 (6.2)	10.1 (6.7)	3.90	0.0003	0.34	0.7368
Fatigue[4]	6.3 (5.0)	7.5 (6.1)	4.2 (5.6)	1.01	0.3189	2.90	0.0056
Confusion[4]	5.3 (3.4)	6.4 (4.0)	5.3 (3.9)	1.98	0.0536	0.24	0.8100

[1] Comparison of B3 and O1.
[2] Comparison of B3 and O2.
[3] From Analogue Mood Scales.
[4] From POMS.

Mean SSS data for the 23 batteries are presented in Figure 10. The ANOVA showed significant main effects of day ($F(2,90) = 24.72$, $p<.0001$) and time ($F(2,90) = 33.99$, $p<.0001$) and a significant day-by-time interaction ($F(4,180) = 34.80$, $p<.0001$). Overall means for B3 and O1 were significantly different but not for B3 versus O2. (See Table 5.) Means for 0900, 1500, and 2100 for each day, collapsed over treatment group, are presented in Figure 10. On O1, reported sleepiness was significantly higher than baseline at 2100 ($t(48) = 11.51$, $p<.0001$). There was no significant difference at 0900 and 1500 on O1. On O2, mean SSS score was significantly lower at 0900 ($t(47) = 3.22$, $p<.0024$) and at 1500 ($t(48) = 3.14$, $p<.0029$) and significantly higher at 2100 ($t(47) = 3.02$, $p<.0041$). (See Figure 11.)

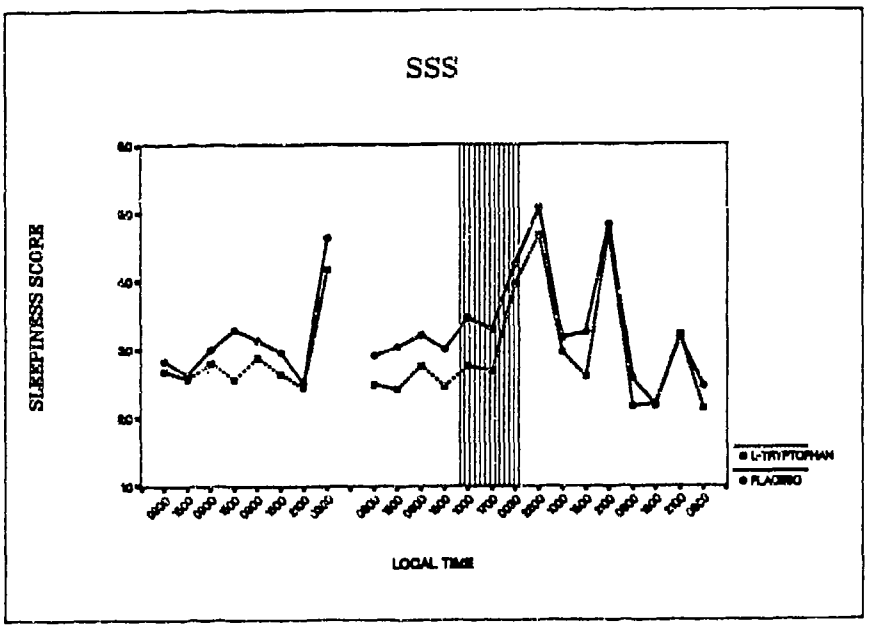


Figure 10. Mean subjective sleepiness on the Stanford Sleepiness Scale (SSS) for the l-tryptophan and placebo groups separately for all test sessions.

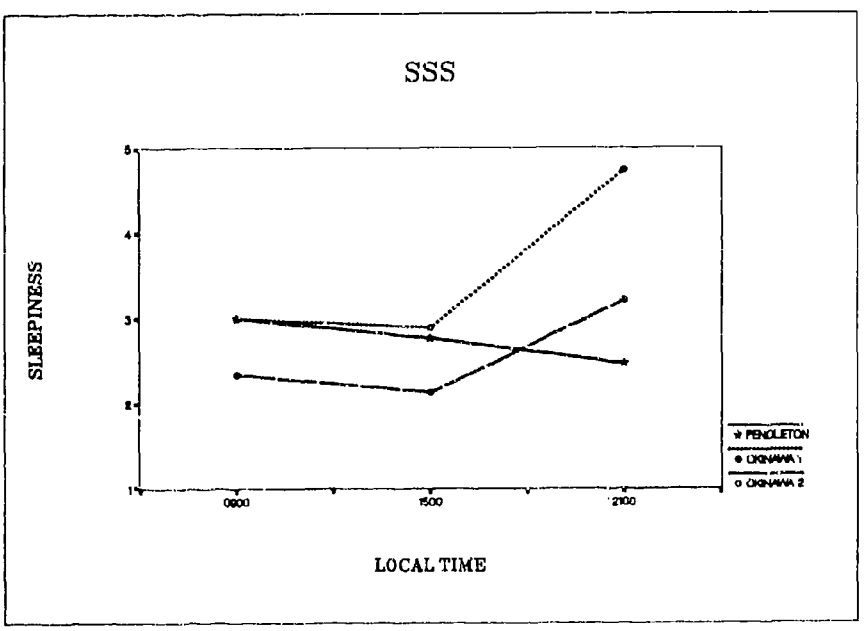


Figure 11. Mean subjective sleepiness on the Stanford Sleepiness Scale (SSS) at 0900, 1500, and 2100 on study days B3, O1, and O2.

Mean reported "effort" for the 23 performance batteries is presented in Figure 12. The ANOVA showed a significant main effect of day ($F(2,74) = 19.15$, $p<.0001$) and time ($F(2,74) = 17.60$, $p<.0001$) and a significant day-by-time interaction ($F(4,148) = 5.62$, $p<.0003$).

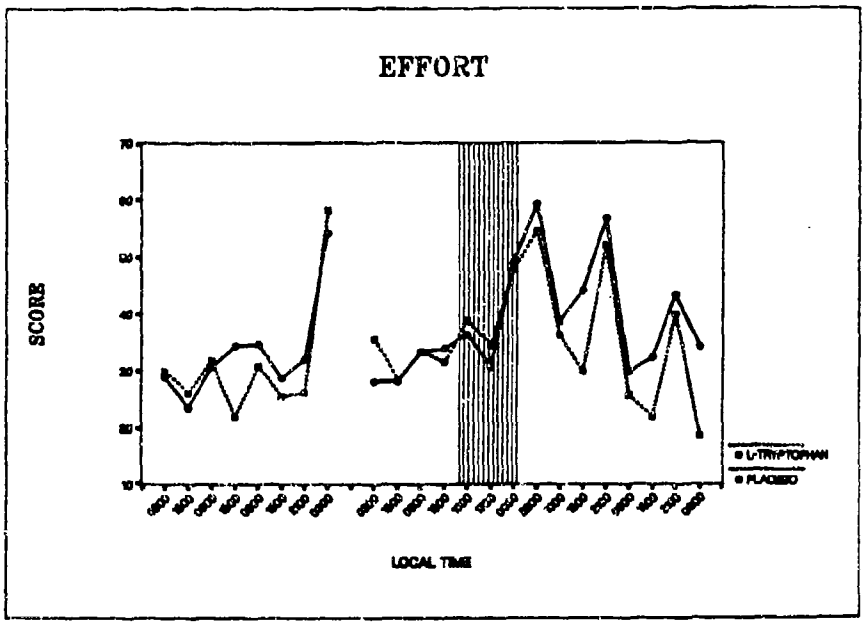


Figure 12. Mean reported "effort" on the Analogue Mood Scales for the l-tryptophan and placebo groups separately for all test sessions.

The overall day mean for 01 was significantly higher than B3. (See Table 5.) Means for 0800, 1500, and 2100, collapsed over groups, are presented in Figure 13. On 01, reported effort was significantly higher at 1500 ($t(48) = 2.33$, $p<.0241$) and at 2100 ($t(47) = 5.54$, $p<.0001$). On day 02, reported effort was still significantly elevated at 2100 ($t(47) = 2.70$, $p<.0095$).

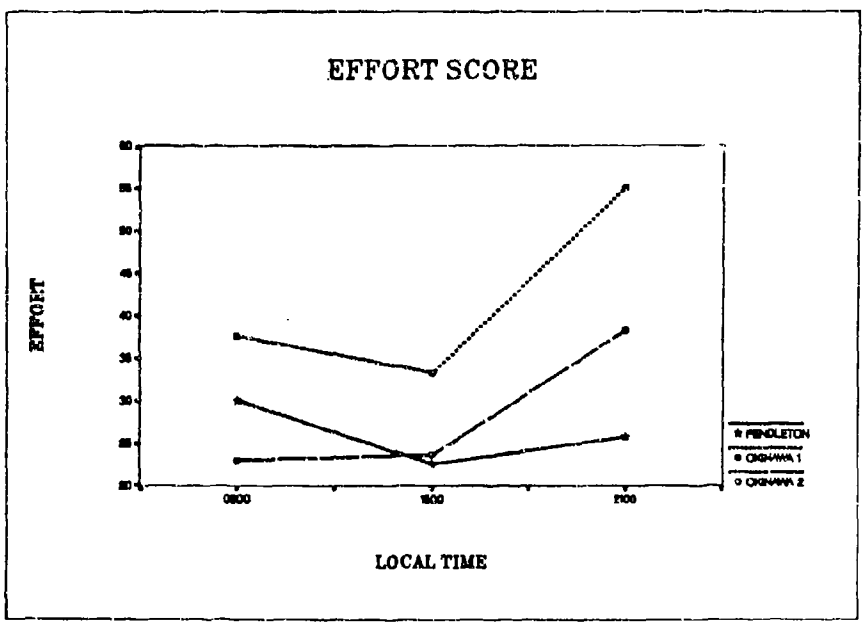


Figure 13. Mean reported "effort" on the Analogue Mood Scales at 0900, 1500, and 2100 on study days B3, 01, and 02.

One subjective scale, "calm" on the AMS, showed no significant F values in the ANOVA and, so, was not analyzed further. Of the 11 remaining subjective measures, these variables all showed significant main effects of day and time, and significant day-by-time interactions: on the AMS, "alert", "sleepy", overall mood; on the POMS, the subscales of depression, anger, and fatigue. The following variables had a significant main effect of day and a significant day-by-time interaction: on the AMS, "sad", "tense", "weary"; on the POMS, confusion. The subscale tension on the POMS only showed a main effect of day.

Analyses of overall day means showed significant differences between O1 and B3 in the expected direction, i.e., on O1, from the AMS, increased sadness, tension, weariness and sleepiness, decreased alertness and happiness, and poorer overall mood; from the POMS, increased depression, tension, anger, confusion, and fatigue, and decreased vigor. On O2, overall day means were not significantly different from B3, except for increased sadness and decreased vigor. (See Table 5.)

From Table 6, we see that, compared to the same time of day on B3 at Camp Pendleton, all mood measures were significantly worse in the evening at 2100 on O1. Certain measures indicated poorer mood throughout the day on O1: these included more sadness, less happiness, more depression and less vigor. By O2, we see that subjective mood was recovering. There was actually less sleepiness reported on the SSS and AMS and more alertness reported than baseline levels at 0900 and 1500. Overall, mood measures were still worse in the evening on O2, but there were fewer statistically significant comparisons with baseline.

For comparison, the overall day means computed according to the biological time approach are presented in Table 7.

DISCUSSION

Major goals of this study of transmeridian flight were to document performance and mood changes and to examine the efficacy of two sleep-enhancing interventions in alleviating acute effects of jet lag.

The environmental controls were very effective in increasing the sleep en route, as objectively measured on Medilog subjects in this operational trial, compared to the pilot subjects studied earlier. The elements of those controls were varied and included timing of activities to maximize uninterrupted sleep periods, control of diet, and administration of a "pill". These manipulations alone increased mean sleep time more than 2 3/4 h compared to mean sleep time of pilot subjects. The l-tryptophan effect aboard the aircraft was not statistically significant, even though the mean increase above placebo was 33 min. In laboratory studies of overnight sleep, a mean increase in total sleep time of over 1/2 h compared to placebo would ordinarily be statistically significant and considered to be substantial. The 52-min increase in total sleep on the first night in Okinawa was considerable, as well. In this case, the difference between l-tryptophan and placebo groups reached statistical significance. There was no sleep-enhancing effect, though, on subsequent nights. It is

important to note that most previous studies reporting positive findings on l-tryptophan emphasized effects on sleep latency rather than total sleep time. In fact, in previous studies, when sleep latency was reported to be reduced, total sleep time was often not statistically increased. In this study in the field, it was impossible to obtain reliable and valid sleep latency measures for individuals and, therefore, we used total sleep time as a measure of sleep-enhancing efficacy. In view of the use of total sleep time rather than sleep-onset time as the dependent measure of efficacy, we are impressed with both the en route and first-night effects.

It may be the case that the absence of sleep-enhancing effects on the second two nights in Okinawa was due to inadequate dose size. On the day of the flight, subjects received two doses of 2 g each, one en route and one after the evening test battery. Our previous sleep laboratory study demonstrating daytime sleep-enhancing effects used a 4-g dose (Spinweber et al., 1983). When we planned this study, we tried to select the smallest effective dose to minimize problems in administration and to avoid the potential side effect of nausea while flying in the aircraft. L-tryptophan, at much larger doses than employed here, is a gastric irritant in some individuals. In consideration of the day of flight data, we may have selected a dose which was too small to augment sleep on the second and third nights.

When we examined the performance and mood data for changes related to sleep enhancement, we were first disappointed that all measures did not reflect treatment-group differences. However, there have been no laboratory studies of sleeping pills and next-day performance which demonstrated enhanced next-day performance in subjects who take the active pill compared with those taking the placebo. (For an extensive review of such studies and a comprehensive discussion of sleeping pills and performance effects, see Johnson and Chernik (1982)). As far as we are aware, then, this study is the first demonstration that improving sleep by psychopharmacological means is associated with enhanced performance on any measure of performance the following day. Perhaps of equal importance, in contrast to sedative-hypnotics, l-tryptophan produced no decrement in performance at any time compared to placebo.

Upon arrival, significant between-groups differences were present only on subjective measures; l-tryptophan subjects reported more alertness and more positive overall mood. But, on O1, after having obtained significantly more nocturnal sleep time (that is, 52 min additional nighttime sleep), the l-tryptophan group differed clearly from the placebo group on one important measure, the faster mean reaction time performance at 2100 on the RT. Probably because it is a longer duration test, RT is very sensitive to sleep-loss effects. The difference between groups on RT showed up at the time of maximal performance loss on several tests, so we are confidant that this RT difference reflects real treatment differences. There is also an indication that STM performance is spared from "jet-lag" effects in the l-tryptophan group on O1. In addition, our data indicate that RT may recover more quickly in l-tryptophan subjects. We also note that our conduct of this operational trial with its emphasis on sleep measures acted to reduce the degree of sleep loss occurring during this deployment, thus minimizing the impact of sleep interventions.

From the data collected in this study, it seems that the second hypothesized jet-lag factor, clock time differences, was a major determinant of acute performance and mood levels following transit. In spite of our notions that the flight itself was especially fatiguing because of its long duration, performance and mood measures upon arrival were quite similar to levels obtained in the middle of the night at Camp Pendleton after approximately 5 h sleep loss. Inspection of the group means for performance measures indicated impaired performance on all tasks except DSST upon arrival, whether the comparison was made with 2100 LT or 0300 LT on B3. For all tasks except short-term memory, inspection of the group means indicated that the battery 16 group mean was more similar to the 0300 mean than to the 2100 mean. When statistical comparisons were made, significant differences were present for AT and RT performance in comparison with battery 7. RT performance was also significantly worse when battery 16 was compared to battery 8. Similarly, on mood measures, levels of alertness or, conversely, sleepiness, were not different than those reported at 0300 LT at Camp Pendleton. As has been previously described in the RESULTS section, other measures more relevant to the psychosocial demands of the airlift were significantly different from 0300 LT data.

Our data indicated that jet-lag effects on both performance and mood were most prominent in the evening in Okinawa. Compared to the performance level at the equivalent BT, AT quickly began to readjust to the new time zone with little performance decrement remaining by the evening on O2. On RT, l-tryptophan subjects adjusted more quickly so that by 2100 LT on O2, the residual deficit was 7.7% in l-tryptophan subjects compared to 19.9% in those receiving placebo. Even though DSST performance was highly influenced by learning over repeated trials, this measure also showed adjustment to LT by O2. In terms of the recovery of mood, we saw a consistent pattern in the various subjective measures of significantly poorer mood and increased sleepiness on O1 particularly in the evening. By O2, mood had recovered in the daytime but was still significantly worse at 2100 compared to B3.

Target shooting accuracy decreased 33% in morning testing. This change suggested that this real world measure may have a different pattern of loss than the other research measures of performance we employed. On DSST, AT, RT, and STM, we did not see 0900 LT or 1500 LT impairments in comparison with baseline data, and, occasionally, we saw relative improvements due to learning curve effects. We wish that we had had the opportunity to obtain repeated measures of target shooting accuracy, particularly at different times of day during baseline and over several days after arrival. It may be the case that, because of so many repeated trials on the research tests during the study, the skills involved were so overlearned that task performance was relatively immune to jet-lag effects. In that case, our findings would underestimate the magnitude of the jet-lag effect on relatively novel types of performance demands. While target shooting should be "overlearned" in Marines, the new range at Okinawa may have presented sufficient novelty to make this performance particularly sensitive to jet-lag effects. We do not know if target shooting accuracy would show a much larger decrement if performance were tested in the evening. A larger decrement at 2100 LT would be consistent with findings from other performance measures.

Our STM data suggested that performance on this task may be the most sensitive to the third jet-lag factor, desynchronosis. In both LT and BT comparisons, performance decrement increased over time

after arrival in Okinawa. As previously mentioned, the data further indicated some l-tryptophan-related sparing of STM performance. A study involving more long-term testing after arrival would be needed to determine how far memory performance deteriorates and when STM performance recovers.

Operational Implications

Our results have important implications for westward rapid deployments having operational demands similar to those occurring in this troop movement. First, the importance of sleep-enhancement cannot be overemphasized. By controlling the aircraft environment and administering l-tryptophan 2 g, the company commander can increase total sleep time en route by over 3 h. L-tryptophan is also effective in enhancing nocturnal sleep after arrival. It is suggested that the appropriate dose for use on the second and third nights after arrival is 4 g.

Second, "jet-lag effects" on performance are problems primarily in the evening and adjustment occurs quickly, for many measures, by the second full day after arrival. Reaction time performance seems to be most sensitive to jet-lag effects and, conversely, to sleep enhancement. If possible, company commanders should avoid nighttime operations on the day of transit and the following day. By the evening of the second full day at destination, the ability to perform calculation quickly and accurately (AT) and decoding performance (DSST) are essentially recovered. Memory performance, though, may continue to deteriorate over the first 3 nights at destination. Our protocol did not extend long enough to identify the time at which short-term memory recovers. Additional justifications for the use of l-tryptophan in the field are that its administration appeared to spare memory to some degree and to hasten readjustment of reaction time performance. The problem of understanding the large decrement in target shooting accuracy has been discussed earlier in this section.

Third, mood upon arrival is generally no worse than would be expected in the middle of the night after a small amount of sleep loss. Throughout the first full day after arrival, mood is poorer than predeployment. If possible, operations requiring positive mood and feelings of alertness and vigor should be scheduled on the second day after arrival.

From both the performance and mood data collected in this study, our conclusion is that military operations would be most effectively conducted in the morning of what would be day 02, the day occurring after 2 nights of sleep and 1 full day at destination. Earlier operations would require compensation for performance impairment in the evenings and impaired mood throughout the first day at destination. The above conclusions would probably hold for similar deployments crossing time zones in the westward direction. Results from other published studies suggest impairment following a similar eastward deployment would be greater and persist longer.

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REPORT DOCUMENTATION PAGE

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1. REPORT NUMBER: 86-15	2. GOVT ACCESSION NO.: AD-A173 482
3. RECIPIENT'S CATALOG NUMBER:	
4. TITLE (and Subtitle): Jet Lag in Military Operations: A Field Trial of L-tryptophan in Reducing Sleep-Loss Effects	5. TYPE OF REPORT & PERIOD COVERED: Preliminary (February 1985 - March 1986)
	6. PERFORMING ORG. REPORT NUMBER:
7. AUTHOR(s): Cheryl L. Spinweber, Schuyler C. Webb, and J. Christian Gillin	8. CONTRACT OR GRANT NUMBER(s):
9. PERFORMING ORGANIZATION NAME AND ADDRESS: Naval Health Research Center, P. O. Box 85122, San Diego, CA 92138-0174	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS: MR041.01.003-0157, MF58.528.002-0001
11. CONTROLLING OFFICE NAME AND ADDRESS: Naval Medical Research & Development Command, Naval Medical Command, National Capital Region, Bethesda, MD 20814	12. REPORT DATE: 21 March 86
	13. NUMBER OF PAGES: 33
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office): Commander, Naval Medical Command, Department of the Navy, Washington, DC 20372	15. SECURITY CLASS. (of this report): UNCLASSIFIED
	15a. DECLASSIFICATION/DOWNGRADING SCHEDULE:

16. DISTRIBUTION STATEMENT (of this Report)

Approved for public release; distribution unlimited.

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

Approved for public release; distribution unlimited.

18. SUPPLEMENTARY NOTES

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

L-tryptophan	Memory	Reaction Time
Sleep	Jet Lag	Target Shooting
Humans	Desynchronosis	
Performance	Time Zone	

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The conduct of military operations may involve rapid deployment across multiple time zones, altered work-rest schedules, and performance under conditions of sleep loss. We evaluated the sleep-promoting effects of the amino acid l-tryptophan in the field in this study of the acute effects of rapid deployments on performance.

-For-

Subjects were 51 Marines (age 21 ± 2.2 years) airlifted from California to Okinawa. Physiological data were obtained from 12 subjects using Medilog re-

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corders. Subjective measures included analog mood scales, the Stanford Sleepiness Scale, and the Profile of Mood States. Performance measures included 4-choice reaction time (RT), an addition task (AT), the Williams Word Memory Test (STM), and the Digit Symbol Substitution Test (DSST). Baseline data were collected 2 weeks prior to deployment on 3 consecutive days (B1, B2, B3), on the 2 days immediately prior to the flight, the day of flight, and 2 days after arrival, (01, 02). Target shooting performance was assessed one week prior to departure and on 01, both sessions at 0800 LT. L-tryptophan 2g or placebo was administered en route and on the first 3 nights in Okinawa. To maximize sleep during flight, environmental interventions included timing of meals and other inflight activities, elimination of caffeine, and control of cabin lighting. Acute "jet lag" effects were assessed by comparing data for B3, 01, and 02 at 0900, 1500, and 2100 LT by ANOVA for repeated measures. Post-hoc t-tests were used to identify sources of significant effects. For target shooting, factors were G and D. Between groups t-tests were used to compare total sleep for l-tryptophan and placebo subjects.

On the first night in Okinawa, total nighttime sleep time was significantly increased in the l-tryptophan group (274.5 $\pm$ 19.9 min vs 222.3 $\pm$ 44.8, t=2.16, p<.0315, one-tailed). Our RT test, a very sensitive measure of fatigue, showed treatment differences with placebo subjects having significantly slower RT at 2100 on 01 (t=2.28, p<.0308, two-tailed). Mean sleep time aboard the aircraft was 291 $\pm$ 79 min for placebo subjects and 324 $\pm$ 146 min for l-tryptophan subjects. This 33-minute difference was not statistically significant. After arrival, evening performance showed the deleterious effects of "jet lag". DSST and AT recovered by 02. STM showed a progressive deterioration from the time of arrival through the evening of 02. There was a consistent pattern in the various subjective measures of significantly poorer mood and increased sleepiness on 01 particularly in the evening. By 02, mood had recovered in the daytime but was still significantly worse at 2100 compared to B3. Target shooting mean scores were significantly lower on 01 (29.2 $\pm$ 10.5 vs 21.2 $\pm$ 9.8, t=4.37, p<.0001, two-tailed).

"Jet lag" may be considered to be the result of multiple factors. Our interventions greatly reduced the impact of sleep loss effects associated with this deployment. The inflight environmental controls increased sleep during transit; data collected earlier in a pilot study showed mean sleep time en route to be only 2 $\pm$ 1.2h, when environmental controls were not employed and no pills were given. L-tryptophan administration increased total sleep time on the first night after arrival, and this increase in sleep was associated with faster reaction time in the evening the following day. As far as we are aware, this study is the first demonstration that improving sleep by psychopharmacological means is associated with enhanced performance the next day. Previous research on westward flight has indicated that readjustment occurs relatively quickly, particularly in young, military subjects. Our data show "jet lag" effects on mood and performance on the first day after arrival with most dramatic decrements in the evening test battery. Many measures show changes which might be interpreted as the beginning of readjustment as early as the second day.